



FEDERAL SECURITY AGENCY

PUBLIC HEALTH SERVICE
DEPARTMENT OF
HEALTH, EDUCATION AND WELFARE

IN REPLYING, ADDRESS THE

Communicable Disease Center
Enteric Bacteriology Laboratories
P. O. Box 183
Chamblee, Georgia

April 15, 1953

BSW 945

Dr. Joshua Lederberg
Department of Genetics
University of Wisconsin
Madison 6, Wisconsin

Dear Dr. Lederberg:

I have not yet read your letter of April 11 but have read your P.S. of April 13, which arrived first. I wish to comment on this before reading further. I should say that the cultures have not been tested and I am taking your statements at face value.

Let us suppose the following: Java N97 is an organism with little or no tendency to phase variation. Yet by good fortune a 1,2 phase was obtained from it. This, like N25 phase 2, behaves genetically as though it were still in phase 1. This may not be illogical since the organism has not undergone normal phase variation (I cling to induction). The 1,2 phase which behaves as phase 1 is replaced by i from *S. typhi* murium. At the same time a factor (gene?) which activates the lost power of phase variation is transferred, as we have seen in other instances. The 1,2 phase of the organism has been replaced by i and since it is normal for the strain to show $b \leftrightarrow 1,2$ variation it now must exhibit $b \leftrightarrow i$ variation. To me this seems rather logical. The only weak point is in the first premise, i.e. the behavior of 1,2 as phase 1. Yet we know from practical experience that this is true. We do not know the reason.

When you speak of N97 -- X *S. miami* I do not know whether you intend using a b or a 1,2 phase. From a b phase, I think you should get $b \leftrightarrow 1,5$, from a 1,2 phase you should get $1,2 \leftrightarrow 1,5$. I do not think you should expect b to act as phase 2. z_{33} acts as a phase 1. This gives some support to 1,2 acting as phase 1 (again induction!).

Perhaps a good approach to this problem would be to determine whether the 1,5 phases of *S. paratyphi* A (of which several are available) act as phase 1. This may be impossible on account of lack of proper phages. However, I think it would be profitable to try. A c phase from *kunzendorf* would also be worth looking at if you had a phage. Would any of Cherry's phages be worth trying?

You could determine whether a phases of *S. abortus equi* obtained in the same way as 1,2 phases of N25 and N97 act as phase 2. I do not recall that you have worked with these. Several are available if you

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want them. I do not know whether a phases obtained by your method would be comparable. Probably they would although they might have more tendency to be resistant to PL22. If you could show that these behaved as phase 2 while 1,2 phases of N25 and N97 behaved as phase 1 it would strengthen my argument. Have you tried to put the latter into S. typhi? They should go in and produce IX,XII: 1,2.

Your last lot of cultures gave us fits and that accounts for the long delay in reporting them. However, I think we have them straight at last.

I have now read your letter of April 11 and I can come to the conclusion only that we are coming closer together in our thinking. I am very strongly of the opinion that j, z₅, z_{3x}, etc. are induced antigens. They represent changes induced in the normal antigens or very minor fractions brought into prominence. Now the only rub is whether a; c; 1,2; and 1,5 phases brought into prominence are merely selected or whether they are induced. I believe this will be hard to prove.

I set up a little experiment with six serums and six kunzendorf strains. Included was Berlin serum absorbed by 958c and Berlin absorbed by 958c,c'. In an attempt to use a uniform inoculum I inoculated the tubes too sparingly. I repeated this today (after having prepared the serum tubes a week ago!). The first experiment indicated that either Berlin serum was effective. More about this later. I will have to repeat this with Berlin absorbed by Berlin boiled and by 958 boiled. This should tell us something. I agree with what you say about the perversity of O agglutinins in migration experiments. Probably it has something to do with whether one is trying to immobilize a dominant antigen which migrates readily or whether one is trying to select a very few bugs which are just becoming established. Also "induced" phases usually aren't too motile when first they appear. I'll let you know the results of my little experiment when it is completed.

We are still manipulating the z₆ phase from S. zega -- X Hines VAH and it still seems monophasic. I am glad you liked the report.

I do not expect to go to the San Francisco SAB meetings. As you know I'm going to Michigan next month and have to go to Oregon for some teaching in July.

I agree the Journal of Immunology would be an excellent medium for publication. I prefer it to Journal of Bacteriology since, like you, I believe we should not stress taxonomic or evolution/implications.

Many thanks for all the aids for the "Lederberg Lecture". I shall return your manuscript next month if that is agreeable. I shudder when I think of what those people in Ann Arbor may hear!

I'm sorry to be so slow in getting the laboratory work done but our situation lately has been somewhat pitiful - staff meetings, continuous visitors, etc., etc. I find nothing in your present shipment that should cause a lot of trouble. We will report as soon as we can.

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I will speak to Bill about the E. coli work and materials. I am confident he will be amenable since some very practical results may be achieved.

We shall send the materials you want so far as possible. I will try to look up the old cultures and will answer your other questions in my next.

I have some S. abortus equi cultures which I want to get out and see if they are normal e,n,x phases. If they are OK I will send them.

With kind regards to you and Esther, I am

For the Officer-in-Charge, Bacteriology Section

Sincerely yours,

Phil

PRE:mg

Philip R. Edwards, Ph. D.
Bacteriologist-in-Charge
Enteric Bacteriology Unit

*Bill is sending the E. coli materials.
We will send the others as soon as possible.
The report on your last previous shipment
is now ready. I will have to write
a letter to accompany it.
P.S. Would you send Fritz Kampmann
a little PL 22 phage + culture? He wants
to try it on X11-2 Para A.*